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ning of each regular issue of the PCT Gazette.

(54) Title: ALBUMIN FUSION PROTEINS

(57) Abstract: The present invention encompasses albumin fusion proteins. Nucleic acid molecules encoding the albumin fusion proteins of the invention are also encompassed by the invention, as are vectors containing these nucleic acids, host cells transformed with these nucleic acids vectors, and methods of making the albumin fusion proteins of the invention and using these nucleic acids, vectors, and/or host cells. Additionally the present invention encompasses pharmaceutical compositions comprising albumin fusion proteins and methods of treating, preventing, or ameliorating diseases, disorders or conditions using albumin fusion proteins of the invention.

WO 01/77137 A1

What is claimed:

1. An albumin fusion protein comprising a Therapeutic protein:X and albumin comprising the amino acid sequence of SEQ ID NO:18.
2. An albumin fusion protein comprising a Therapeutic protein:X and a fragment or a variant of the amino acid sequence of SEQ ID NO:18, wherein said fragment or variant has albumin activity.
3. The albumin fusion protein of claim 2, wherein said albumin activity is the ability to prolong the shelf life of the Therapeutic protein:X compared to the shelf-life of the Therapeutic protein:X in an unfused state.
4. The albumin fusion protein of claim 2, wherein the fragment or variant comprises the amino acid sequence of amino acids 1-387 of SEQ ID NO:18.
5. An albumin fusion protein comprising a fragment or variant of a Therapeutic protein:X, and albumin comprising the amino acid sequence of SEQ ID NO:18, wherein said fragment or variant has a biological activity of the Therapeutic protein:X.
6. The albumin fusion protein of any one of claims 1-5, wherein the Therapeutic protein:X, or fragment or variant thereof, is fused to the N-terminus of albumin, or the N-terminus of the fragment or variant of albumin.
7. The albumin fusion protein of any one of claims 1-5, wherein the Therapeutic protein:X, or fragment or variant thereof, is fused to the C-terminus of albumin, or the C-terminus of the fragment or variant of albumin.
8. The albumin fusion protein of any one of claims 1-5, wherein the Therapeutic protein:X, or fragment or variant thereof, is fused to the N-terminus and C-terminus of albumin, or the N-terminus and the C-terminus of the fragment or variant of albumin.

9. The albumin fusion protein of any one of claims 1-5, which comprises a first Therapeutic protein:X, or fragment or variant thereof, and a second Therapeutic protein:X, or fragment or variant thereof, wherein said first Therapeutic protein:X, or fragment or variant thereof, is different from said second Therapeutic protein:X, or fragment or variant thereof.

10. The albumin fusion protein of any one of claims 1-8, wherein the Therapeutic protein:X, or fragment or variant thereof, is separated from the albumin or the fragment or variant of albumin by a linker.

11. The albumin fusion protein of any one of claims 1-8, wherein the albumin fusion protein has the following formula:

R1-L-R2; R2-L-R1; or R1-L-R2-L-R1,

wherein R1 is Therapeutic protein:X, or fragment or variant thereof, L is a peptide linker, and R2 is albumin comprising the amino acid sequence of SEQ ID NO:18 or fragment or variant of albumin.

12. The albumin fusion protein of any one of claims 1-11, wherein the shelf-life of the albumin fusion protein is greater than the shelf-life of the Therapeutic protein:X in an unfused state.

13. The albumin fusion protein of any one of claims 1-11, wherein the in vitro biological activity of the Therapeutic protein:X, or fragment or variant thereof, fused to albumin, or fragment or variant thereof, is greater than the in vitro biological activity of the Therapeutic protein:X, or a fragment or variant thereof, in an unfused state.

14. The albumin fusion protein of any one of claims 1-11, wherein the in vivo biological activity of the Therapeutic protein:X, or fragment or variant thereof, fused to albumin, or fragment or variant thereof, is greater than the in vivo biological activity of the Therapeutic protein:X, or a fragment or variant thereof, in an unfused state.

15. An albumin fusion protein comprising a Therapeutic protein:X, or fragment or variant thereof, inserted into an albumin comprising the amino acid sequence of SEQ ID NO:18 or fragment or variant thereof.

16. An albumin fusion protein comprising a Therapeutic protein:X, or fragment or variant thereof, inserted into an albumin comprising an amino acid sequence selected from the group consisting of:

- (a) amino acids 54 to 61 of SEQ ID NO:18;
- (b) amino acids 76 to 89 of SEQ ID NO:18;
- (c) amino acids 92 to 100 of SEQ ID NO:18;
- (d) amino acids 170 to 176 of SEQ ID NO:18;
- (e) amino acids 247 to 252 of SEQ ID NO:18;
- (f) amino acids 266 to 277 of SEQ ID NO:18;
- (g) amino acids 280 to 288 of SEQ ID NO:18;
- (h) amino acids 362 to 368 of SEQ ID NO:18;
- (i) amino acids 439 to 447 of SEQ ID NO:18;
- (j) amino acids 462 to 475 of SEQ ID NO:18;
- (k) amino acids 478 to 486 of SEQ ID NO:18; and
- (l) amino acids 560 to 566 of SEQ ID NO:18.

17. The albumin fusion protein of claims 15 or 16, wherein said albumin fusion protein comprises a portion of albumin sufficient to prolong the shelf-life of the Therapeutic protein:X, or fragment or variant thereof, as compared to the shelf-life of the Therapeutic protein:X, or a fragment or variant thereof, in an unfused state.

18. The albumin fusion protein of claims 15 or 16, wherein said albumin fusion protein comprises a portion of albumin sufficient to prolong the in vitro biological activity of the Therapeutic protein:X, or fragment or variant thereof, fused to albumin as compared to the in vitro biological activity of the Therapeutic protein:X, or a fragment or variant thereof, in an unfused state.

19. The albumin fusion protein of claims 15 or 16 wherein said albumin fusion protein comprises a portion of albumin sufficient to prolong the in vivo biological activity

of the Therapeutic protein:X, or fragment or variant thereof, fused to albumin compared to the in vivo biological activity of the Therapeutic protein:X , or a fragment or variant thereof, in an unfused state.

20. The albumin fusion protein of any one of claims 1-19, which is non-glycosylated.

21. The albumin fusion protein of any one of claims 1-19, which is expressed in yeast.

22. The albumin fusion protein of claim 21, wherein the yeast is glycosylation deficient.

23. The albumin fusion protein of claim 21 wherein the yeast is glycosylation and protease deficient.

24. The albumin fusion protein of any one of claims 1-19, which is expressed by a mammalian cell.

25. The albumin fusion protein of any one of claims 1-19, wherein the albumin fusion protein is expressed by a mammalian cell in culture.

26. The albumin fusion protein of any one of claims 1-19, wherein the albumin fusion protein further comprises a secretion leader sequence.

27. A composition comprising the albumin fusion protein of any one of claims 1-26 and a pharmaceutically acceptable carrier.

28. A kit comprising the composition of claim 27.

29. A method of treating a disease or disorder in a patient, comprising the step of administering the albumin fusion protein of any one of claims 1-26.

30. The method of claim 29, wherein the disease or disorder comprises indication:Y.

31. A method of treating a patient with a disease or disorder that is modulated by Therapeutic protein:X, or fragment or variant thereof, comprising the step of administering an effective amount of the albumin fusion protein of any one of claims 1-26.

32. The method of claim 31, wherein the disease or disorder is indication:Y.

33. A method of extending the shelf life of Therapeutic protein:X comprising the step of fusing the Therapeutic protein:X, or fragment or variant thereof, to albumin or a fragment or variant thereof, sufficient to extend the shelf-life of the Therapeutic protein:X, or fragment or variant thereof, compared to the shelf-life of the Therapeutic protein:X, or a fragment or variant thereof, in an unfused state.

34. A nucleic acid molecule comprising a polynucleotide sequence encoding the albumin fusion protein of any one of claims 1-26.

35. A vector comprising the nucleic acid molecule of claim 34.

36. A host cell comprising the nucleic acid molecule of claim 35.